

**ALASKA MEDICAID
PHARMACY AND THERAPEUTICS COMMITTEE**

**Location of Meeting
Frontier Building, 3601 C Street, Room 890/896**

**FINAL MINUTES OF MEETING
November 16, 2007
8:00 a.m.**

Committee Members Present:

Marvin Bergeson, MD
Heidi Brainerd, MS R.Ph
Amber L. Briggs, Pharm.D
Richard E. Brodsky, MD
Robert H. Carlson, MD (telephonic)
Kelly C. Conright, MD
Lucy Curtiss, MD
Jeffrey G. Demain, MD
Traci Gale, Pharm D.
Vincent Greear, R.Ph.
Daniel P. Kiley, DDS, MPH
Diane Liljegren, MD (telephonic)
Gregory R. Polston, MD
Sherrie D. Richey, MD (telephonic)
Janice L. Stables, MSN, ANP (telephonic)
Trish D. White, R.Ph. (telephonic)

Committee Members Absent:

Mark D. Bohrer, R.Ph
Andrzej Maciejewski, MD
R. Duane Hopson, MD

Others Present:

David Campana, R.Ph.
Melinda Sater, Pharm D, First Health

1. Call to Order – Chair

The meeting was called to order at 8:14 a.m.

2. Roll Call

A quorum was present.

3. Public Comment – Local Public/Local Physicians

Jan Adaisiak: A psychiatric nurse practitioner at the Anchorage Community Mental Health Services advocated for the broadest access possible to all psychiatric medications. The mental health centers are specialty care venues for the mentally ill. They deal with high acuity patients who often have several diagnoses, often with a history of treatment resistance. They have co-morbidities such as traumatic

brain injuries, substance abuse, diabetes, heart disease, and hypertension. These patients are more difficult to treat than patients in the private sector. Restricting access to these drugs would be similar to restricting drug access to an oncologist at a cancer center.

Alexander von Hafften: a psychiatrist in Anchorage said the committee focused on two major issues: enhancing the quality of care given with evidence-based medicine, and enhancing access to care by maximizing the utilization of the financial resources available. Any medication is available by writing medically necessary. The committee has supported the grandfather clause in the past and should continue to do so. Depression is one of the most highly prevalent medical conditions and the fourth leading cause of disability worldwide. It is especially common in patients with chronic medical problems, which affects adherence to treatment regimens as well as health related behaviors. According to Group Health, about 42% of patients will discontinue antidepressants within the first month of treatment and 72% within three months of treatment. The majority of depression is evaluated and treated in the primary care setting. We need to differentiate between effectiveness and efficacy. The STAR-D Trial was reviewed. About 50% of patients will respond with the first trial of any medication and 15-35% will reach remission. In steps 2-5, the evidence-based medicine doesn't guide us very well. There are incremental improvements regarding response and remission. Unless the comorbidities and bio-psycho social, cultural and spiritual aspects of the individual are considered, it is likely remission will not be reached. Regarding the SSRIs, there is a class effect. However, that does not mean the SSRIs are interchangeable within a given patient. There are important differences that relates back to difference between efficacy and effectiveness. At least three SSRI should be on the PDL, including Lexapro and/or Sertraline. For the SNRIs, Venlafaxine and Duloxetine, which are classified together, are different as reflected in the side effect profiles. Other Antidepressants contain a number of medications that have different mechanisms. The difference between long-acting versus short-acting preparations goes back to the differences between effectiveness and efficacy. The fewer times a person has to take a medication, the more likely they are to adhere to the recommended plan and the less likely they are to have adverse side effects. For the Sedative/Hypnotic class, he recommended at least one non-benzodiazepine. For the attention deficit/hyperactivity disorders, there should be at least one each of the long-acting and one short-acting methylphenidate and amphetamine compounds. He encouraged continuing Strattera on the PDL. For the Anticonvulsants, there should probably be multiple medications available. For Bipolar disorders, limiting these medications increases the likelihood of using Lithium or Atypicals, which both have their positives and negatives.

Verner Stillner: An adult general psychiatrist said he worked in a public facility as well as community health centers throughout Southeast Alaska. He thanked the committee for the choices available on the PDL. Regarding the SSRIs, 15% of Alaskans have no health insurance. Lexapro has provided the mental health centers with adequate stocks so uninsured patients can have an affordable SSRI available to them. Lexapro is the cleanest in terms of the P-450 to interact with other psychotropic drugs and should be included on the PDL. Regarding the SNRIs, Effexor XR and Cymbalta should both be retained on the PDL. In terms of Hypnotics, Rozerem should be included on the PDL, as it does not have a danger of addiction for chemically dependent patients. My child psychiatrist colleagues believe Daytrana should be included for the ADD population, because it is the only patch methylphenidate available and decreases the chances of it being diverted, misused or abused. For the Anticonvulsants used in the bipolar spectrum, Lamictal is a highly desirable drug for people that are increasing their weight burden and metabolic syndrome potential and should be included on the PDL.

Dr. Hugh Starks: A physician with Counseling Solutions of Alaska said his patient population was 50-60% Medicaid patients from Denali Kid Care. He advocated for an open formulary and access. He reviewed his experience and credentials. Focalin is an extended release methylphenidate. Extended release has several advantages when treating patients. As a methylphenidate salt, it has the same safety as all methylphenidates. One size does not fit all and we need an open formulary for each patient. An extended release medication allows for once-a-day administration, which enhances compliance. Often children do not get their medications at home. We have signed on with the Anchorage School District allowing them to administer the medications at school so the children receive the proper doses. There are three subtypes of ADHD and one size does not fit all. Focalin can be taken once a day. It is front-end loaded and has an immediate release drug that is available within an hour. By giving a child the medication between 7:30 or 8:00 o'clock, by 9:00 o'clock, when he is in class, he is able to function for up to 12 hours on a single dose. The 12 hours is important, because the child needs to be able to function during the school day and in the early evening for homework or other activities. It also reduces the chaos within the home. Clinically, we know that children who are focused have less aggression. Co-morbidity is also an issue and includes a broad spectrum of problems. Focalin is safe, can be dosed once daily, can be adjusted, and we have good clinical experience with it. An open formulary is important and should be given a priority.

4. Review of COX II Inhibitors

David Gross: A representative from Pfizer Medical discussed Celebrex. In 2004, cardiovascular data from the APPROVe Trial resulted in the voluntary withdrawal of Vioxx from the market. This led to a thorough review of the safety data of both the COX II Inhibitors and non-selective nonsteroidal anti-inflammatory products. In February of 2005 after extensively reviewing this data, the FDA Advisory Committee voted 31-to-1 that the overall risk benefits profile for Celebrex supported its continued marketing in the United States. They also said it wasn't possible to conclude that the Cox II selective drugs confer an increased cardiovascular risk over the non-selective nonsteroidals in chronic use. This led to changes in packaging inserts and black box warnings for all these types of medications. Several trials were reviewed. While the possibility of a class effect exists, there is no evidence to support this and there has been evidence to refute it. The Safety and Regulatory Committee at the FDA rejected a new product, because it failed to meet the burden of scrutiny. In addition to the safety data, unlike the non-selective nonsteroidals, Celebrex does not have an effect on platelet function and does not diminish the anti-platelet effect of aspirin.

Dr. Sater gave the First Health presentation on COX II Inhibitors. Celebrex and Meloxicam are being considered, although Meloxicam is only COX II specific at lower doses. The indications are varied, but the efficacy and adverse drug reaction profiles are very similar. In October there were 303 claims: 80% for Celebrex and 20% for Meloxicam. This is a new class, so there was no previous discussion. Dr. Michael Mas (ph) feels Celebrex should be added to the PDL for use in patients unable to take other NSAIDs, those on aspirin therapy, and patients with other issues.

Dr. Demain said Celebrex was the only COX II inhibitor that was tolerated by aspirin sensitive patients. Although it was not in the FDA report, it is well studied.

DR. LILJEGREN MOVED A CLASS EFFECT. SECONDED BY DR. POLSTON.

Dr. Conright questioned considering this a class effect. It was previously noted that Meloxicam was only COX II specific at lower doses.

In response to Dr. Conright, Dr. Sater said Meloxicam had been around long enough to be a generic so providers should be able to make the adjustment or the medically necessary clause could be used.

Dr. Polston discussed the side effects of Celebrex and noted that a new cardiovascular side effect had appeared. Celebrex is a very expensive drug to use frequently. However, if we can get a price advantage, there are indications and aspirin sensitive people who get relief with Celebrex at reasonable doses. However, very high doses of Celebrex are not COX II specific and COX I affects start appearing with higher doses.

Dr. Brodsky felt Celebrex was overused, was no better than NSAIDs, and the side effect profile, which was touted as being safer, was not. However, patients are using Celebrex, so we will save money if the motion is approved.

THE MOTION PASSED WITH 1 OPPOSED.

5. Re-review of Proton Pump Inhibitors

JUDI MAR-BURBIDGE: A clinical marketing manager with TAP Pharmaceuticals discussed Prevacid. The PPI class provides symptomatic relief of GERD and they all share a degree of acid suppression. According to HEDIS guidelines, it does not matter what the efficacy studies show if the patients are not compliant with the medical therapy. With the introduction of Medicare Part D, the Medicaid patient base is predominately geared toward single mothers with children and compliance can be an issue. Prevacid has shown an efficacy of up to 95% in healing erosive esophagitis in adults. Safety in pregnancy is a category B. Prevacid is the only branded PPI that has an indication for pediatrics of ages 1 through 11, and a study shows 100% efficacy after 12 weeks in healing of erosive esophagitis. Children are often unable to verbalize their complaints to their caregivers. Refusal of medications and progression of youth GERD symptoms will increase healthcare dollars and hospitalization. Prevacid has many administrative options, which increases compliance.

Dr. Sater gave the First Health presentation on Proton Pump Inhibitors. There are five available entities, six branded products and generic Omeprazole. The FDA approved indications vary, but in clinical practice all of the drugs are used for all indications. Adverse drug reaction profiles and efficacy are similar. The preferred agents are Nexium and Prevacid capsules. In October there were 3,024 claims: 34% for Nexium, 28% for Prevacid, 26% for generic Omeprazole, 5% for Protonix, 3.5% for Prevacid Rapid Tabs, and less than 3% for the remainder. At the last review there was limited discussion regarding adding of generic products to the PDL as soon as possible and the need for alternate dosage forms for children and G-2 patients. A motion for a class effect passed unanimously. There have been no significant changes in this class since the last review.

Dr. Demain said proton pump inhibitors were the treatment of choice in many of the acid related diseases. We deal with many children and are having high success with Prevacid specifically. Due to its varied dosage forms, as well as its approval and use in young children and pregnant women, Prevacid should be included on the PDL.

Dr. Richey said all proton pump inhibitors were used during pregnancy.

DR. DEMAIN MOVED TO DECLARE A CLASS EFFECT, WITH ALL FORMS OF PREVACID BEING INCLUDED PREFERENTIALLY. SECONDED BY DR. CONRIGHT.

Dr. Greear felt a class effect should be declared, but did not believe all form of Prevacid was necessary. Prevacid is a good drug, but does not have any great advantages over the other drugs.

Dr. Liljegren agreed with the class effect, but felt that only one Prevacid preparation, for pediatrics, was necessary.

Dr. Demain suggested adding an age restriction of 12 years old on the motion.

Dr. Conright felt there was a broader range of age populations that could benefit from Prevacid, but was not sure if all of the dosage forms were necessary.

THE MOTION PASSED WITH 6 OPPOSED.

6. Re-review of Histamine₂-Receptor Antagonists

There were no public testimonies.

Dr. Sater gave the First Health presentation on Histamine₂-Receptor Antagonists. There are four available agents and they are all pretty much the same. The drug interaction of Cimetidine is cause for concern. Currently, Ranitidine and Famotidine are preferred. In October there were 690 claims: 72% for Ranitidine, 17% for Famotidine, and less than 10% for the rest of the class. During the last review, there was limited discussion. The motion to declare a class effect, excluding Cimetidine preferentially due to drug interactions, passed unanimously.

DR. BERGESON MOVED TO DECLARE A CLASS EFFECT, EXCLUDING CIMETIDINE. SECONDED BY DR. CONRIGHT.

Dr. Demain felt a pediatric suspension or syrup should be included in the motion.

DR. DEMAIN MOVED TO ADD A PEDIATRIC SUSPENSION OF SYRUP TO THE PDL. SECONDED BY DR. BERGESON.

THE MOTION TO AMEND THE MOTION PASSED WITH 2 OPPOSED.

THE MOTION TO APPROVE THE MOTION, AS AMENDED, PASSED UNANIMOUSLY.

7. Re-review of Urinary Tract Antispasmodics

Fred Amberger: A regional scientific director with Novartis discussed Enablex. Enablex is a potent M3 muscarinic receptor antagonist that has been shown to be safe and effective in the treatment of OAB. The vitro studies with Enablex show that it has a much greater affinity for the M3 receptors than for the other known muscarinic receptors. When treating patients with OAB, consideration needs to be

given to the fact that very often these patients are elderly with co-existing cardiovascular disease. Enablex has been studied in this population. Several studies were discussed. CNS effects should also be considered in this population and include memory deficits, sleep disruption, confusion, or hallucinations. Enablex has been studied to determine its impact on memory in healthy individuals. In the study, it did not affect memory recall in healthy individuals when compared to placebo. Enablex has also demonstrated long-term bladder control. It is the only OAB drug to have long-term, open labeled data published to date. In a two-year study, it was reported that the efficacy of Enablex increased from 63% at 12 weeks to 84% at two years with no increase in adverse events. Enablex has been shown to be safe and effective. The most common adverse events are dry mouth and constipation. Serious adverse events for Enablex at dosages at 7.5 milligrams and 15 milligrams are comparable to placebo.

Leigh Platte: A scientific liaison with Astellas discussed VESicare for over active bladder. In this patient population, the goal of therapy is to get the patient dry with a minimum of side effects. In our registration trials of over 18,000 people, 51% of the patients were dry. The rate of dry mouth was less than 11% at the 5-milligram dose. In the one-year trial, 81% of patients were still on the drug at the end of the calendar year. The half-life of this drug is about 50 hours, so you get good 24-hour control. The STAR study was discussed in which the secondary endpoints tended to favor Solifenacin, including the patient's perception of their own bladder condition. The VENUS trial was discussed. Urgency is the most bothersome symptom for these patients and often curtails their activities. During the study, the voiding time was measured and the difference was an additional 31 seconds with VESicare. In every VESicare trial, at least half the patients were dry at 12 weeks and willing to stay on the drug for a period of time, because it was well tolerated with a reasonable side effect profile.

David Gross: A clinical education manager for Pfizer discussed Detrol. This class was reviewed 10 months ago and over that time the market share was 50% for Detrol LA, 15% for generic Oxybutynin, and the remaining 35% between the other products. There are no real head-to-head trials that show any superiority of any of the products over Detrol LA. A head-to-head study that compared Detrol LA to Ditropan XL demonstrated superiority for Detrol LA. The side effects differences with Detrol LA and Oxybutynin were reviewed. Dry mouth and constipation were much greater with Oxybutynin than Detrol LA. In the adherence literature, there are about six published claim analyses that compared Detrol LA with Oxybutynin and showed there were consistently higher persistence rates with Detrol LA. In light of the fact that Detrol LA is currently on the PDL and the provider community in Alaska has preferred this product, Detrol LA should remain on the PDL.

Dr. Sater gave the First Health presentation of Urinary Tract Antispasmodics. There are five available chemical entities, nine products both branded and generic, and one transdermal product. There is similar efficacy across the class, although the adverse drug reaction profiles do differ. There is better patient tolerability with the new agents versus Oxybutynin. In October there were 388 claims: 52% for Detrol LA, 12% for VESicare, 11% for Enablex, 9% for generic Ditropan XL, 7.5% for Oxybutynin, and the remainder for the rest of the agents. During the last review, there was no discussion. The motion to include Detrol LA and other agents as identified in the bid process passed unanimously. Since the last review, generic Ditropan XL has come to the marketplace. The Alaska Southcentral Urology specialists prefer Detrol LA for their patients.

Dr. Lillegren MOVED A CLASS EFFECT WITH ONE LONG-ACTING ORAL FORM BEING INCLUDED. THERE WAS NO SECOND.

In response to Dr. Bergeson, Dr. Sater said no statistics on children were provided. The only agent approved for children is Oxybutynin.

Dr. Conright said overactive bladder was generally a condition of the elderly and side effects are very important. She was concerned that with a class effect, there may be a preference for something with a higher side effect profile.

DR. CONRIGHT MOVED A CLASS EFFECT, BUT THERE BE AT LEAST ONE NEWER AGENT PREFERRED. THERE WAS NO SECOND.

The committee discussed other ways to phrase the motion. Dr. Sater said last year's motion was to include Detrol LA and whatever other agents fell out in the bid process, which passed unanimously. Detrol LA was included due to provider support. Currently the preferred agents are Detrol LA, VESIcare, Enablex, and generic Oxybutynin immediate release.

DR. BERGESON MOVED A CLASS EFFECT, BUT INCLUDE AT LEAST TWO AGENTS. SECONDED BY DR. BRIGGS.

Dr. Liljegren recommended included an oral long-acting agent.

DR. DEMAIN MOVED TO AMEND THE MOTION TO INCLUDE AT LEAST ONE ORAL LONG-ACTING AGENT AMONG THE CLASS EFFECT DRUGS. SECONDED BY MR. GREAR. THE REQUEST TO AMEND THE MOTION PASSED UNANIMOUSLY.

THE MOTION, AS AMENDED, PASSED UNANIMOUSLY.

8. Review of Growth Hormones

Donna King: The senior medical research specialist for Pfizer discussed Genotropin by discussing four points that differentiate Genotropin from the other drugs. Pfizer has extensive clinical experience with our clinical surveillance database. There is a wide range of indications. There is a wide range of injection devices. And there is comprehensive patient support program. The databases serve as a resource for physicians and researchers that include many non-typical patients. Genotropin has five indications including children small for gestational age and Prader-Willi Syndrome. Only Genotropin can provide comprehensive patient or parent education materials for these two conditions and Pfizer does that in both English and Spanish. We have a large selection of pen delivery devices for the injectable Genotropin including the mini-quick device. This device is a disposable, single-use device that requires no refrigeration and is ideal for children who are shuttled between caregivers. It is also the simplest device on the market, which makes it ideal for people who are challenged by complex devices, are arthritic or blind. The patient support program is state of the art and facilitates both the prescription process and patient training to increase compliance with the injection regimen for Genotropin.

Kay Leslie: A former registered nurse and a regional clinical coordinator with Genentech discussed Nutropin and Nutropin AQ. Nutropin has indications in pediatric growth hormone deficiency, adult growth hormone deficiency, chronic renal insufficiency in pediatrics, Turner Syndrome and idiopathic

short stature. We have two label extensions that are unique including puberal dosing and improvement of bone mineral density for adult patients. We have the only indication for chronic renal insufficiency. Genentech was the first company to develop growth hormones by recombinant DNA technology. Nutropin AQ is a premixed solution and Nutropin is a powdered form, which can be mixed in varying amounts to help the physicians adjust the volume of medication for the patient. Nutropin AQ, since it is premixed, takes less time to prepare and administer. It does not contain benzoalcohol as a preservative, which is important because benzoalcohol cannot be used in a neonatal setting. It is simple and easy to use. We have a personalized reimbursement support system that assists patients in the authorization process, documentation submission, appeals and recertification. Nutropin should be considered for the PDL.

Dr. Marks: The growth hormone molecule itself is the same regardless of what company you get it from. However, we do not just prescribe growth hormones, but an entire package that includes everything from the device, refrigeration needs, the availability of free drugs while insurance issues are being taken care of, and other concerns. The degree of support is highly variable from company to company. When we begin limiting companies, we take away choices. Our patients are at a disadvantage if they are put on a low budget package. He encouraged the committee to look beyond the growth hormones and also consider the entire package.

Belinda Burtcett: A medical liaison for Novo Nordisk discussed Norditropin. In June of this year, Norditropin was pleased to announce that it received U.S. Food & Drug Administration approval for the treatment of short stature and Noonan Syndrome. We are the only growth hormone therapy for Noonan Syndrome. We also received the indication for Turner Syndrome this year, as well as the two previous indications of pediatric and adult growth hormone deficiency. The NordiPen is the only premixed, pre-filled, multi-dose, disposable pen delivery device with storage flexibility. It is easy to use and easy to train. It requires no loading, mixing or changing of cartridges. The 5- and 10-milligram cartridges can be kept at room temperature for three weeks. Norditropin also provides comprehensive support services, breaching the gap during transition between therapies and reenrollment periods of Medicaid patients. We have experience in converting patients from other products by in-home injection training. We have a jump start on medication, on a short-term basis, for patients in need. The addition of Norditropin means improving the quality of care for the Alaska Medicaid population.

Dr. Sater gave the First Health presentation on Growth Hormones. This is a new class for PDL review. There are a number of different products that are all exactly the same molecule. The indications and delivery devices vary between the different agents. In October there were 11 claims: 55% for Genotropin and 45% for Nutropin or Nutropin AQ. Dr. Wendy Bailey, who works at the Children's Hospital at Providence, feels that Genotropin should be added to the PDL. She states the unique delivery device, indications for both SGA and Prader-Willi Syndrome and the Bridge Patient Compliance Monitoring Program make Genotropin a superior product. There are very stringent and extensive criteria that must be met for access growth hormones for patients.

In response to Dr. Polston, Mr. Campana said there has been a prior authorization requirement for growth hormones since the Federal Medicaid Program began. Patients must fit strict criteria to receive growth hormones and the drugs are somewhat expensive. The decision to require a prior authorization probably came from the former medical director.

DR. POLSTON MOVED A CLASS EFFECT. SECONDED BY DR. CONRIGHT.

In response to Ms. Burtcett, Dr. Sater explained the prior authorization process. When the provider calls for a preauthorization, they are asked if they want to use the preferred drug or something else, but they always get to prescribe whichever drug they want to use.

THE MOTION PASSED UNANIMOUSLY.

9. Re-review of Long Acting Opioids

Joe Burt: A representative for Endo Pharmaceuticals discussed Opana ER. Last year, we received FDA approval for the new oral extended release formulation of the Opioid Oxymorphone, which bring the number of oral extended release Opioid products on the market to three. Substantial clinical evidence exists showing that different patients with the same condition might respond differently to the same Opioid. It has been recently shown that there may be numerous mu-receptor subtypes and different Opioid molecules have different activation capabilities at a given receptor subtype. Since it is not possible to predict which patients will respond to any particular Opioid, practitioners will need to have several unique Opioid molecules. The addition of extended release Oxymorphone to the PDL provides patients and practitioners with an effective option. Opana ER has been formulated in the Time RX delivery system, which is designed to provide consistent levels of Oxymorphone over a 12-hour dosing period. This consistent dosing has been demonstrated in the Opana ER clinical program. Several studies were reviewed.

Dr. Sater gave the First Health presentation on Long Acting Opioids. There are four available chemical entities. There are four oral morphine dosage forms that are all different, oral Oxycodone, and transdermal Fentanyl. Opana is new to this class. All are mu-receptor antagonists with the same mechanism of action, similar efficacy and side effect profiles. Pharmacokinetic parameters differ between the products. Many products carry and black box warning regarding extreme potency, abuse potential, and overdose of patients. In October there were 576 claims: 29% for generic Morphine extended release, 18% for generic duragentic patches, 17% for OxyContin, 17% for general OxyContin, 11.5% for Kadian, 4.5% for Avinza, and less than 4% for the remaining drugs. There was limited discussion at the last review regarding the use of long-acting narcotics for long-term use in patients. The motion for a class effect, preferentially excluding Atiq, and including at least one oral medication, passed unanimously.

Dr. Polston said there was an emphasis in the use of Opioids for pain control. We believe the long-acting agents provide more sustained relief. There is about a 30% reduction in pain with Opioid so it is very effective. With safety profile, compared to the COX II, they are probably one of the safest medications used with the exception of risk of abuse or misuse. The question is whether exposing people to Opioids cause a substance abuse disorder or whether the substance abuse disorder was already present. Unlike other classes that have a high rate of patients who stop using the medications, Opioids patients never stop, because they work very well when used appropriately. The true difference in the long-acting medications is the delivery systems and whether they have a short-acting component. There is a lot of argument as to how or when these medications should be used. Pain is very difficult to measure and each patient is different. Dr. Polston felt this was a class effect.

In response to Dr. Briggs, Dr. Polston said he would like to have access to all of these medications for his practice. The transdermal patch is effective and may be more difficult to abuse. Compared to other states, our use of this category is actually very good.

Dr. Sater said generic MS Contin, Kadian, Duragesic and Oramorph were currently preferred agents.

Dr. Polston said his main concern was the limits on Opioids and how that came about. He felt the limits were arbitrarily set and enacted very quickly without a lot of discussion within the community.

DR. KILEY MOVED A CLASS EFFECT. SECONDED BY DR. POLSTON.

DR. DEMAIN MOVED TO AMEND THE MOTION TO INCLUDE AT LEAST ONE TRANSDERMAL AND ORAL FORMULATION. SECONDED BY DR. BERGESON.

The committee discussed whether the motion should be amended to include at least one Morphine product and one Methadone product.

DR. LILJEGREN MOVED TO AMEND THE MOTION TO INCLUDE AT LEAST ONE LONG-ACTING MORPHINE AND METHADONE PRODUCT ON THE PDL. THERE WAS NO SECOND TO THE MOTION.

Dr. Polston discussed prior authorizations and noted that requests for long-acting Opioids have been denied in the past. He was confused about what the committee was actually voting on.

Mr. Campana said preferred drugs that required prior authorization was somewhat complicated. With a preferred drug that requires a prior authorization, those that get the drugs are limited with an established medical need within appropriate time limits. All the Opioids were brought under prior authorization this summer to keep their utilization to appropriate levels. There is literature that advocates keeping patients at moderate or appropriate doses and we are trying to do that with the prior authorization. It has been challenging to work with the preferred list and the prior authorization.

Dr. Polston noted that the preauthorization system had not always worked smoothly and he was not sure where those decisions were made.

Mr. Campana said this topic should be addressed under the Drug Utilization Review to insure that it works in conjunction with the PDL.

THE MOTION TO AMEND THE MOTION PASSED UNANIMOUSLY.

THE MOTION, AS AMENDED, PASSED UNANIMOUSLY.

10. Review of Fentanyl, Buccal

There were no public testimonies.

Dr. Sater gave the First Health presentation on Fentanyl, Buccal. We are only considering only Fentanyl products, both Buccal and Transmucosal. All agents currently require a prior authorization.

They are for use only in Opioid-tolerate patients. They have a single FDA approved indication, which is management of breakthrough cancer pain and patients already receiving Opioids. In October there were 3 claims: 2 for Fentora and 1 for branded Atiq.

In response to Dr. Briggs, Dr. Sater said utilization has decreased significantly since the prior authorization was required.

DR. BERGESON MOVED A CLASS EFFECT. SECONDED BY DR. BRIGGS. THE MOTION PASSED UNANIMOUSLY.

11. Re-review of Antidepressants, Selective Serotonin Reuptake Inhibitors (SSRIs)

Jake Knee: A regional manager with Forest Labs discussed Lexapro. Lexapro is currently the only agent in the SSRI class that is currently being promoted and sampled to physicians in the community. We are continuing to invest in research and clinical trials to further the wealth of data we already have on Lexapro. There are currently 31 clinical trials that have been conducted, 17 of which are head-to-head. Six of those are directly versed the SNRIs. Lexapro is the number one prescribed antidepressant in the world in long-term care, new starts in neurology, new starts in psychiatry, new starts in primary care. One of the primary reasons it is number one in long-term care is its safety and tolerability profile. In all 31 of the clinical trials there has never been a comparator group that had fewer dropout rates or fewer side effects, with the exception of the placebo trials. The FDA gave us approval to mark a placebo-like side effect profile in our marketing pieces. At 10 milligrams, Lexapro has a 4% dropout rate compared to 3% on placebo. Like all antidepressants, Lexapro has side effects, but overall it has the cleanest side effect profile. Several studies were reviewed. Patients should have access to the most tolerable and safest antidepressant, which is Lexapro. We will also continue to support providers with samples, as well as our Patient Assistance Program.

Dr. Sater gave the First Health presentation of Antidepressants, Selective Serotonin Reuptake Inhibitors (SSRIs). There are six available chemical entities including extended release, immediate release, and various dosage forms. There is one combination product, which we will not be considering in this class. Minuet affinities for other receptors vary between the agents and may account for subtle differences in adverse drug reactions. The efficacy is similar across all agents in this class. In October there were 3,363 claims, 13 of which were for liquids. The currently preferred agents are Fluoxetine, Paroxetine, Citalopram and branded Zoloft. In previous discussions, the importance of having at least one drug with fewer adverse effects and drug interactions was discussed. Having one agent for use in pediatrics was discussed, as was the automatic addition of generic products to the PDL as soon as they are available. The motion to include at least three SSRIs, one of which must be Citalopram, Escitalopram or Sertraline, and adding liquid Fluoxetine to the PDL, passed with one opposed. There have been no significant changes to this class since the last review. Dr. Hopson feels that there is class effect for this group. Dr. Curtiss prefers to use Citalopram, Sertraline or Escitalopram, because those agents have fewer drug interactions. Dr. Bergeson said he prefers Escitalopram and thinks his patients experience fewer adverse drug reactions with that product.

DR. CURTISS MOVED TO INCLUDE AT LEAST THREE SSRIs, ONE OF WHICH MUST BE CITALOPRAM, ESCITALOPRAM OR SERTRALINE, AND LIQUID FLUOXETINE TO THE PDL. SECONDED BY AN UNIDENTIFIED MALE. THE MOTION PASSED UNANIMOUSLY.

12. Re-review of SNRIs

Dr. Sater noted that last year the SNRIs and the other antidepressants were considered together.

13. Review of Antidepressants, Other

Christian Linn: A representative of the medical division of Eli Lilly & Company discussed Cymbalta. Cymbalta is indicated for the treatment of major depressive disorder, generalized anxiety disorder, and diabetic peripheral neuropathic pain. Remission should be the goal of antidepressant therapy and it is important to treat patients to full remission to avoid higher risks of relapse. Clinical trials for Cymbalta demonstrated remission rates of 43-44% as compared to 16% and 29% for placebo. It demonstrated a rapid onset as early as one or two weeks. However, according to the APA antidepressant efficacy, it may take up to 4 to 6 weeks or more in some patients. Cymbalta has demonstrated efficacy in treating the painful physical symptoms associated with depression with significant improvements in overall pain severity as early as the second week. The data suggests that depressed patients with lingering, painful physical symptoms are associated with greater total medical costs, compared to depressed patients without pain. Several studies were reviewed. Cymbalta is not indicated for the treatment of children or adolescents. It should not be used in any patients with hepatic insufficiency, chronic liver disease, end stage renal disease, a patient with substantial alcohol abuse, or in combination with MAOI's. Cymbalta should be included on the PDL.

Dr. Sater gave the First Health presentation on Antidepressants, Other. There are six available chemical entities. There are many different products, both extended release and immediate release. Their mechanisms broadly vary. The adverse drug reactions are also widely varied. However, efficacy across the agents is similar. In October there were 3,013 claims: 26% for Trazodone, 22% for Cymbalta, 21% for Effexor XR, 12% for Wellbutrin XL, 6% for Mirtazapine, 4% for generic Wellbutrin XL, 3.5% for generic Wellbutrin, 1% for generic Effexor immediate release, and less than 3% for the rest of the agents. Currently preferred are Trazodone, Cymbalta, Effexor XR, Wellbutrin XL, Mirtazapine, generic Wellbutrin immediate release, generic Effexor immediate release, generic Wellbutrin SR, nefazodone, and Mirtazapine. Previous discussion included the importance of having extended release preparations. The meaning of a class effect and the mission of the committee were discussed, as were the many off label uses for drugs in this class. The motion to include at least one product from every chemical entity, and all available extended release products, and branded Wellbutrin XL, passed with two opposed. Since the last review, generic Wellbutrin XL has been added to the market. Dr. Hopson prefers using long-acting agents in this class. Dr. Curtiss uses all of the long-acting agents. Dr. Bergeson uses Effexor and Wellbutrin for the long-acting agents.

In response to Dr. Curtiss, Dr. Sater said when generics were first approved there is a 6-month exclusivity period where they are very expensive. Over 9 to 12 months, the prices of generic products decrease. In the initial 6-month period, we are often in a position where it is more financially responsible to prefer a branded product to a generic product. After 9 to 12 months, the prices will level out.

In response to Dr. Conright, Dr. Sater explained the rationale for including branded Wellbutrin XL. There were some on the committee who felt that saying all extended release preparations did not adequately address the issue, so they included branded Wellbutrin XL.

The committee discussed whether it would be better to separate the SNRIs and the other antidepressants.

DR. CURTISS MOVED TO INCLUDE ONE PRODUCT FROM EACH CHEMICAL ENTITY, TO INCLUDE THE ONCE A DAY PRODUCTS WHEN THERE IS A CHOICE, AND ALL AVAILABLE EXTENDED RELEASE PRODUCTS. SECONDED BY DR. CONRIGHT. THE MOTION PASSED WITH 5 OPPOSED.

14. Re-review of Sedative Hypnotics

Eric Taylor: A local physician representing Takeda discussed Rozerem. The mechanism of action for Rozerem was discussed. It is FDA approved for insomnia. It has been shown to decrease sleep latency and increase total sleep time both in transient and chronic insomnia patients. Rozerem is available in a single 8-milligram dose, which covers a wide range of patients. Dosage adjustments are generally not required. The only cautionary use for Rozerem would be for someone who has moderate hepatic insufficiency. Rozerem has not been widely studied in COPD or severe respiratory disorders. In Alaska, Rozerem's effects through its melatonin receptor agonist on circadian rhythms may be unique and important due to our unusual light and dark conditions. Rozerem is the only drug in the class that is not considered a controlled substance. It has a very low risk for dependency abuse, tolerance or withdrawal. In working with insomnia medicine, Rozerem is a very important tool for me.

Dr. Jon Sonota: A medical scientist for Sanofi Aventis discussed Ambien CR. It is indicated both sleep induction and maintenance. The World Health Organization says anyone who has insomnia symptoms for two weeks is considered chronic, whereas the National Institute of Health says anyone who has symptoms for four weeks is considered chronic. That means primary insomnia rarely exists, but by the time a patient come to see a doctor, they will be diagnosed as having chronic insomnia. Benzodiazepines are only indicated for 7 to 10 days or short-term use. Zolpidem and Zaleplon were indicated for 10 to 14 days. You need a product that can be used for chronic patients. Several studies were reviewed. The National Institute of Health's statement on sleep says the best form of therapy for long-term use for chronic insomnia is non-benzodiazepines used in combination with CBT.

Dr. Sater gave the First Health presentation of Sedative/Hypnotics. There are 10 available entities in this class, both extended and immediate release. There are two broad categories within this class, benzodiazepines and non-benzodiazepines. Rozerem has a unique mechanism in this class. In October there were 1,125 claims: 33% for Ambien CR, 25% for generic Ambien immediate release, 19% for Temazepam, 15% for Lunesta, 13% for Rozerem, 3% for Triazolam, 3% for branded Cambien, and less than 2% for the rest. The current preferred agents are Ambien CR, Temazepam, Triazolam, Estazolam, Flurazepam and Rozerem. In previous discussions, the benzodiazepine and non-benzodiazepine agents were considered separately. There was a limited discussion on the potential advantages of Rozerem over other agents in this class. The motion to include at least one benzodiazepine and one non-benzodiazepine, and preferentially include Rozerem, passed unanimously. Since the last review, generic Ambien has been added to the market. Dr. Curtiss uses Rozerem in her practice. She also uses some Ambien immediate release and a small amount of Lunesta. Dr. Hopson uses primarily Temazepam in his practice. Dr. Ann. Morris uses Rozerem, Ambien CR, and Lunesta. She states the unique mechanism of Rozerem makes it particularly useful in certain patients. She feels

Ambien CR and Lunesta are superior to older agents in safety and efficacy measures. Dr. Bill Light would like to see Ambien and Ambien CR retained on the PDL as he feels they are superior agents.

Dr. Conright felt that if benzodiazepines were included in the motion then an agent with a short duration of action should be included for safety reasons for the elderly population.

DR. CURTISS MOVED TO INCLUDE AT LEAST ONE BENZODIAZEPINE, AT LEAST ONE NON-BENZODIAZEPINE, AND ROZEREM. SECONDED BY DR. GALE. THE MOTION PASSED UNANIMOUSLY.

15. Re-review of Stimulants and Related Agents

Tracy Durgin: A regional scientific director with Novartis discussed Focalin XR. Treatment of ADHD is not one size fits all. Recent treatment guidelines have indicated the need to individualize treatment for these patients. Depending on the dosage form or the delayed release mechanism, different patients respond differently to different treatments. Focalin XR is an extended release formulation. It utilizes technology releasing 50% of the drug immediately upon ingestion and 50% approximately four hours later. Focalin XR is the first and only methylphenidate preparation given once daily that is FDA approved for children, adolescents and adults. It has a rapid onset of action, taking effect within 30 minutes of ingestion, which means that parents no longer have to wake their children up two hours before breakfast in order for their drug to take affect. In addition, it lasts for 12 hours. The capsules can be opened up and sprinkled onto food for those who are unable to take oral medications. We respectfully request that Focalin XR be maintained on the PDL.

Christian Linn: A representative of the medical division of Eli Lilly & Company discussed Strattera. ADHD is highly co-morbid with other disorders. These co-morbidities can impact treatment selection as well as treatment outcome. While stimulants are considered a first line therapy when no co-morbidities are present, Atomoxetine may be considered as the first medication for ADHD persons with an active substance abuse problem, co-morbidity anxiety or ticks. Adult patients are more likely to have received Atomoxetine if they have a prior diagnosis of Bipolar disorder, anxiety, alcohol dependence or previous antidepressant use. Children are more likely to have received Atomoxetine than a long-acting stimulant if they had prior diagnoses of anxiety disorders, alcohol dependence or ticks. 7.3 million persons, age 12 or older, report misusing ADHD stimulants in their lifetime. From 1993 to 2005, the rate of abuse of prescription stimulants rose 93%. Between 2004 and 2005, emergency room visits associated with non-medical use of Methylphenidate rose 108%. In undergraduate college students, the ratio of medical to illicit use of stimulate ADHD medication by young adults was a ratio of 2.5 to 1. Overall safety and tolerability of Strattera has been demonstrated in clinical trials. However, the Strattera package insert includes boxed warnings regarding an increased risk of suicide, risk of severe liver injury, and allergic conditions. In 2006, the label was updated to include other issues. Strattera should not be taken within two weeks of an MAOI. Additional information is available in the Strattera PI, which can be provided.

Dr. Sater gave the First Health presentation on Stimulants and Related Agents. There are eight available entities with both extended and immediate release products, as well as one transdermal preparation. Provigil does not have a pediatric indication. Strattera has a unique non-stimulant mechanism of action. These agents are used in both adults and children. Approximately 11% of the claims in this class were for adults. There is similar efficacy among all agents in this class, but much

variability in patient response. In October there were 1,977 claims: 27% for Concerta, 18% for Adderall XR, 15% for Strattera, 8.5% for Focalin XR, 5.5% for Provigil, 5.5% for generic Amphetamine salt combinations, 5% for Methylin, 3% for general Methylphenidate immediate release, and less than 10% for the remainder. The currently preferred agents are Concerta, Adderall XR, Strattera, Focalin XR, general Amphetamine salt combination, Methylin, Ritalin LA, Dextroamphetamine tablets, Dextroamphetamine capsules, Metadate CD, Focalin, Methylin ER, Methylphenidate ER, DextroStat, and Metadate ER. The previous discussions centered on the importance of having both long- and short-acting products on the PDL, in addition to Strattera due to its non-stimulant mechanism. Preferentially excluding Methamphetamine was also mentioned. Lack of evidence suggesting superiority of one product over another was briefly discussed. The motion to include an immediate release and an extended release Methylphenidate, preferentially including Concerta; immediate release and extended release mixed amphetamine salts; extended release and immediate release Dexmethylphenidate and Strattera, passed with three opposed. Since the last review, generic Focalin immediate release and Vyvanse has been added to the marketplace. Dr. Bergeson feels that extended release products are preferable. He would like to see immediate release and extended release Methylphenidate, immediate release and extended release Dextroamphetamine, and Strattera maintained on the PDL. Dr. Curtiss uses Strattera in her practice.

In response to Dr. Conright, Dr. Sater said Concerta was preferred last year, probably because it was the most commonly used Methylphenidate product and people felt there was a nice pharmacokinetic parameter associated with it and it lasts for 12 hours.

DR. BERGESON MOVED TO INCLUDE A SHORT-ACTING AND LONG-ACTING METHYLPHENIDATE PRODUCT, PREFERRING CONCERTA; A SHORT-ACTING AND LONG-ACTING DEXTROAMPHETAMINE PRODUCT; AND STRATTERA. SECONDED BY DR. DEMAIN.

The committee discussed Provigil.

DR. BERGESON AMENDED THE MOTION TO INCLUDE PROVIGIL. SECONDED BY DR. POLSTON. THE REQUEST TO AMEND THE MOTION PASSED WITH 3 OPPOSED.

THE MOTION, AS AMENDED, PASSED WITH 3 OPPOSED.

16. Re-review of Anticonvulsants, 1st and 2nd Generation

David Gross: A representative with Pfizer discussed Lyrica. This class was reviewed a year ago and was included on the PDL. Since that time, the FDA has awarded Lyrica a new indication for the management of fibromyalgia, which is a common and widespread pain condition that include tenderness, sleep disturbance, fatigue and morning stiffness. Several studies were reviewed. Last year the committee saw the value of Lyrica in treating with seizure and neuropathic pain, and I hope also see its value in the management of fibromyalgia and continue to make it available on the PDL.

Jennifer Brzana: A representative for GlascoSmithKline discussed Lamotrigine, which was currently on the PDL. Lamotrigine was introduced in the United States in 1994 as an effective adjunctive therapy option for the treatment of refractory partial seizures in adult patients. Since that time, indications have expanded to include adjunctive therapy for refractory partial seizures in children

greater than age 2, the treatment of generalized seizures associated with Lennox-Gastaut Syndrome in adults and children, conversion to monotherapy for partial seizures in adults, and adjunctive therapy for the treatment of primary generalized seizures in adult and children down to the age of 2. All these indications allow Lamotrigine to be considered among the few broad-spectrum anti-epileptic drugs available for the treatment of seizure disorder. Only Lamotrigine has been proven to extend stability by delaying time to occurrence of both depressive and manic episodes in adults with Bipolar disorder. For providers, Lamotrigine has a favorable pharmacokinetic profile and blood monitoring is not required. It is not metabolized or an inducer or inhibitor of the P-450 system so there is a low likelihood that it would affect the metabolism of other drugs. It has the longest running pregnancy registry in existence. For patients, Lamotrigine has a very favorable tolerability profile. The most common adverse events reported included dizziness, headache, blurred vision and insomnia. Studies in both epilepsy and bipolar have shown Lamotrigine to have a weight neutral affect. In studies in both epilepsy and bipolar, they have shown that Lamotrigine has no significant clinical impact on cognitive domains including memory, attention and concentration, cognitive and motor speed, and language. Prescribing information contains a box warning concern serious rashes. Utilizing appropriate starting doses and titration can minimize the risk. Lamotrigine's broad indications, favorable pharmacokinetics and tolerability profile, along with combined clinical evidence, make it a favorable candidate for the PDL.

Dr. Sater gave the First Health presentation on Oral Anticonvulsants. This is a widely varied group with a lot of drugs. There are 17 different chemical entities. There are many dosage forms. There are a number of mechanisms in this class and some are not completely understood. Adverse drug reactions and efficacy is also quite varied. The currently preferred agents were reviewed. In October there were 4,215 claims. At the last review, there was discussion about the widely varied group and how difficult it was to grasp as a class so no one felt a class effect was appropriate. There were two motions. The first motion was for the Carbamazepine-like groups, Oxcarbazepine was preferentially included, along with whatever else fell out, in pediatric and adult forms; for Valproic Acid, a pediatric and adult formulations, as well as Phenytoin products was included. The second motion was to preferentially include a Gabapentin product and Lyrica. Since the last review, two generic products have been released. Dr. Hopson uses mostly Depakote, typically the XR product. He also said Lamictal and Topamax are useful as mood stabilizers. Gabapentin is sometime used as well. Dr. Hopson would like at least one agent from each mechanism on the PDL. Dr. Curtiss felt Oxcarbazepine, Lamotrigine, and Depakote ER were important for mood stabilization. Dr. Wayne Downs and Dr. Mary Downs believe that all anticonvulsants need to be on the PDL due to significant inter-patient variability and response to different agents.

Dr. Liljgren felt it was difficult not to include all the drugs, because not only were they used for seizures, but for off label uses as well.

Dr. Sater said in October there were 4,215 claims: 16.5% for generic Gabapentin, 14.5% for Topamax, 12% for Lamictal, 12% for Trileptal tablets, 7.5% for Depakote ER, 7% for Depakote, 5% for generic Carbamazepine, 5% for Keppra, 4% for Lyrica, almost 3% for branded Dilantin, almost 3% for Tegretol XR, 2% for Depakote sprinkles, 1.5% for Carbatrol, and less than 6% for the rest.

Dr. Sater said if the same motion were made as last year, 7 of the top 10 drugs in this class would be preferred.

Dr. Liljegren felt Topamax should be included, because it was used for migraines, mood stabilization, and seizures.

Ms. Brainerd noted that with 4,215 claims, whatever was done in this class would significantly impact their financial resources. All the drugs are available by utilizing the medical necessity clause.

DR. BERGESON MOVED THAT ALL THE DRUGS WERE CLINICALLY EFFECTIVE AND TO INCLUDE AT LEAST OXCARBAZEPINE IN PEDIATRIC AND ADULT FORMS; A VALPROIC ACID-LIKE DRUG IN PEDIATRIC AND ADULT FORMS; PHENYTOIN IN PEDIATRIC AND ADULT FORMS; GABAPENTIN AND LYRICA. SECONDED BY MS. STABLES.

DR. LILJEGREN MOVED TO AMEND THE MOTION TO INCLUDE TOPAMAX BE INCLUDED ON THE PDL. SECONDED Dr. Demain. THE AMENDMENT FAILED WITH 8 OPPOSED.

THE MOTION FAILED WITH 10 OPPOSED.

MS. BRAINERD MOVED THAT A CLASS EFFECT COULD NOT BE DECLARED IN THE ANTICONVULSANT REVIEW DUE TO THE MULTIPLE CLINICAL INDICATIONS THAT THESE MEDICATIONS ARE USED FOR AND, AS SUCH, WE ACCEPT THE BID AS RECEIVED. SECONDED BY MS. GALE. THE MOTION PASSED WITH 1 OPPOSED.

17. Review Minutes from September 28, 2007

Mr. Campana said there were no changes to the minutes.

DR. KILEY MOVED TO APPROVE THE SEPTEMBER 28, 2007, MEETING MINUTES AS WRITTEN. SECONDED BY DR. BERGESON. THE MOTION PASSED UNANIMOUSLY.

18. Final Comments by Chair or Other Members

Mr. Campana said the next meeting would be January 18, 2008, and the classes to be reviewed were discussed. The following meeting would be April 20, 2008.

Dr. Demain discussed the results of a previous meeting. Albuterol had been removed from the PDL and Xopenex got the bid, but they were not determined to be interchangeable. So every Albuterol prescription had to be rewritten. Making these types of changes to the PDL creates confusion and has an impact on patients. In that particular case, we created a disservice to our medical community and patients. We need some type of safety net for when those types of things happen. We should fix that particular problem today. When you see a drug that is prescribed 95% of the time, you cannot just vote it away. If we determine a class effect, the drugs should be interchangeable.

The committee discussed the issue. Dr. Brodsky said the drugs in the class were therapeutically equivalent and changing the PDL to include a drug that submitted a higher bid than another drug would undermine the whole process. Dr. Demain said changing drugs caused confusion with patients.

Dr. Bergeson asked for clarification on prior authorization for PPIs.

Mr. Campana said the DUR Committee instituted the prior authorization for PPIs. We were concerned about utilization and continual use among numerous patients. If the guidelines were adhered to, we would not have to do that. To be fiscally responsible and to maintain appropriate care, we felt it was best to add the prior authorization. We had intended to implement this in 2006, but due to confusion in the system, it has not yet been done. Two letters were sent out advising prescribers that the PPIs would require prior authorizations in the future.

Dr. Demain said the PPIs were now drugs of choice. We are looking at over 3,000 prescriptions and it is a lot of work to get prior authorizations. He noted that the approvals probably would not be declined and questioned why physicians had to go through the process.

Dr. Conright said care was becoming more fragmented all over the country. With new patients, the physician may not always be aware of why certain medications were started so they are reluctant to discontinue them.

The committee discussed patient medications at the time of discharge from a hospital, which they often don't need as an outpatient. The primary care provider should review the list of medications for a patient and determine which ones they need to use on a continuing basis.

Dr. Polston discussed the process. He has served on the DUR Committee for several years and there has never been a good discussion on why prior authorizations were required. The role between the DUR Committee and this committee should be evaluated and we need more information on how prior authorizations or limits are set.

Dr. Brodsky recommended suggesting to the DUR Committee to remove the prior authorization requirement on the PPIs.

Mr. Campana said he appreciated the comments and would take them under advisement.

The committee further discussed the issue and the impact it would have in certain areas.

The meeting adjourned at 11:59 p.m.